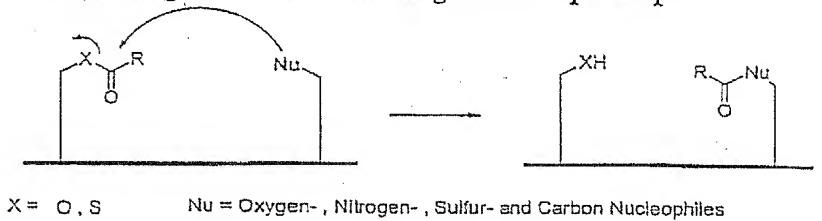
Fig. 6. Reaction types allowing simultaneous reaction and linker cleavage.

Nucleophilic substitution using activation of electrophiles

FIG. 6A. Acylating monomer building blocks - principle



Acylation

FIG. 6B.

Amide formation by reaction of amines with activated esters



FIG. 6C. Acylation

Pyrazolone formation by reaction of hydrazines with β -Ketoesters

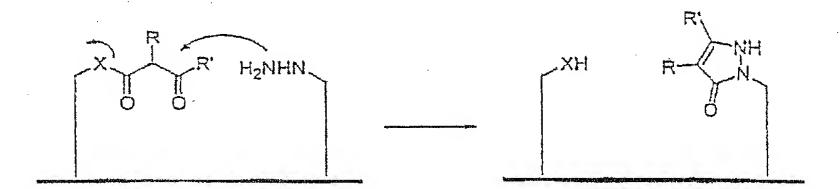


FIG. 6D. Acylation

Isoxazolone formation by reaction of hydroxylamines with β -Ketoesters



FIG. 6E. Acylation

Pyrimidine formation by reaction of thioureas with β -Ketoesters

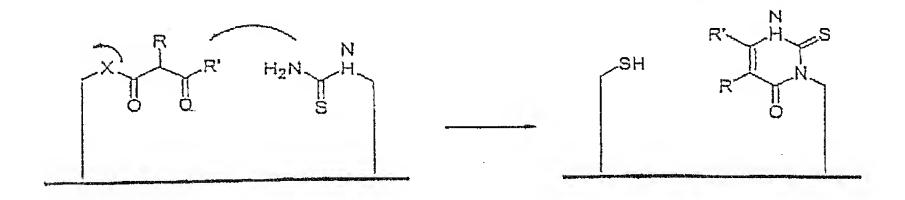


FIG. 6F. Acylation

Pyrimidine formation by reaction of ureas with Malonates

FIG. 6G. Acylation

Coumarine or quinolinon formation by a Heck reaction followed by a nucleophilic substitution

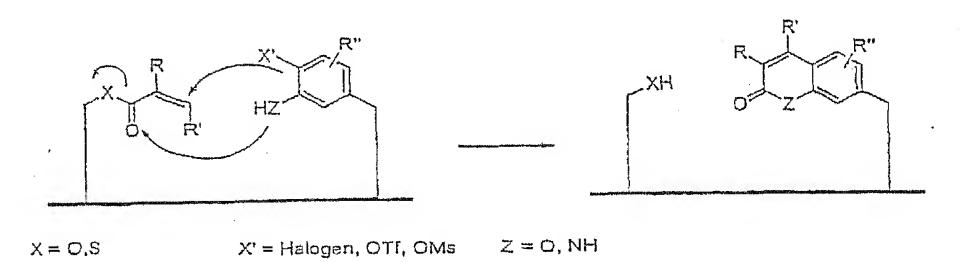


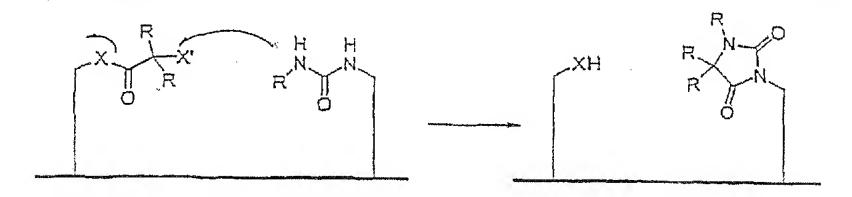
FIG. 6H. Acylation

Phthalhydrazide formation by reaction of Hydrazines and Phthalimides

FIG. 6I. Acylation

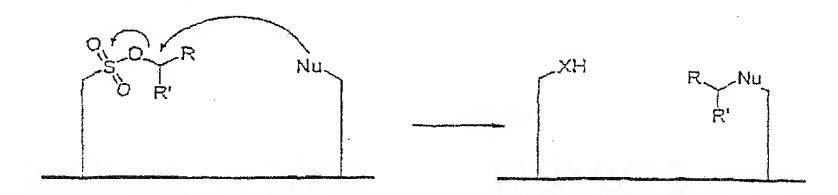
Diketopiperazine formation by reaction of Amino Acid Esters

FIG. 6J. Acylation Hydantoin formation by reaction of Urea and α -substituted Esters



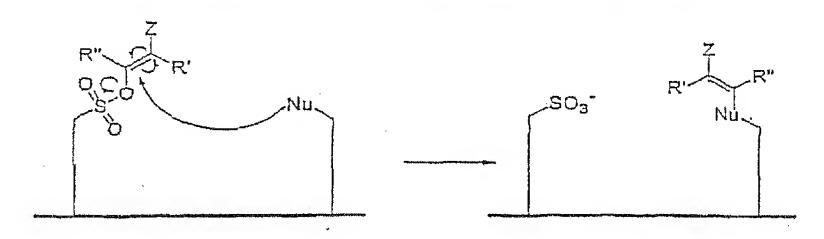
X = O, S X' = Hal, OTos, OMs, etc.

FIG. 6K. Alkylating monomer building blocks - principle Alkylated compounds by reaction of Sulfonates with Nucleofiles



Nu = Oxygen-, Nitrogen-, Sulfur- and Carbon Nucleophiles

FIG. 6L. Vinylating monomer building blocks - principle



Z = CN, COOR, COR, NO₂, SO₂R, S(=0)R, SO₂NR₂, F Nu = Oxygen-, Nilrogen-, Sulfur- and Carbon Nucleophiles

FIG. 6M. Heteroatom electrophiles

Disulfide formation by reaction of Pyridyl disulfide with mercaptanes

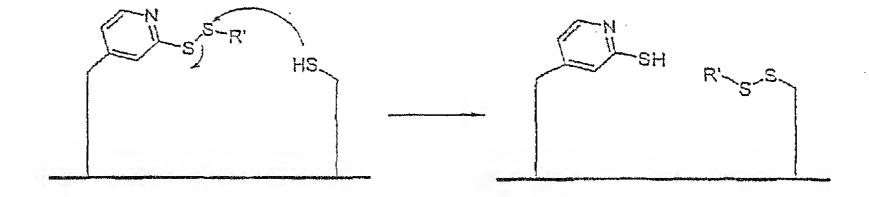


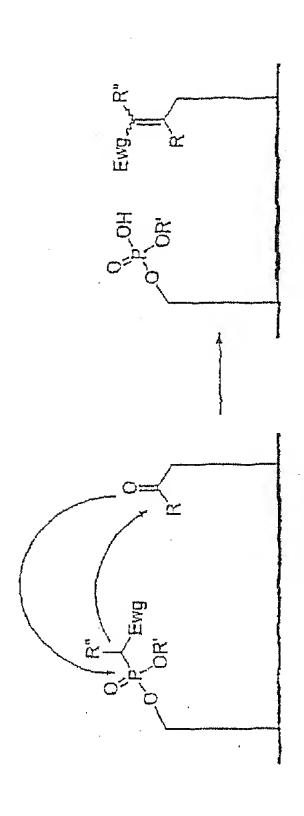
FIG. 6N. Acylation

Benzodiazepinone formation by reaction of Amino Acid Esters and Amino Ketones

S'O=X

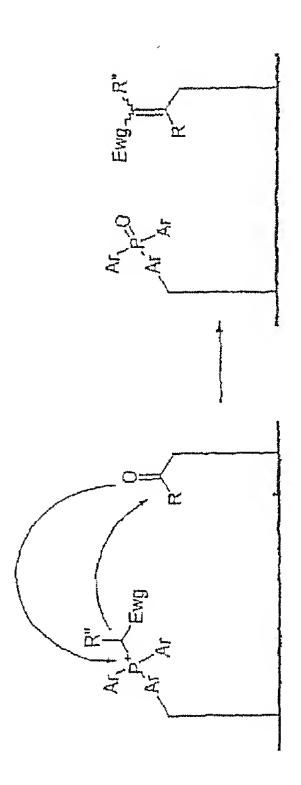
Addition to carbon-hetero multiple bonds

FIG. 60. Wittig/Horner-Wittig-Emmons reagents Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones



Ewg = CN, COOR, COR, NO2, SO2R, S(=0)R, SO2NR2, F etc

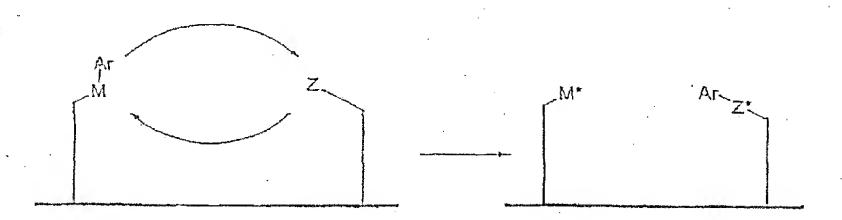
FIG. 6P. Wittig/Horner-Wittig-Emmons reagents Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones



Ewg = CN, COOR, COR, NO₂, SO₂R, S(=0)R, SO₂NR₂, F etc. Ar = aryf, hetaryl

Transition metal catalysed reactions

FIG. 6Q. Transition metal cat. Arylations



Z = haloaryl, halohelaryl, ArOMs, ArOTI, ArOTos or NHR or OH or SH etc.

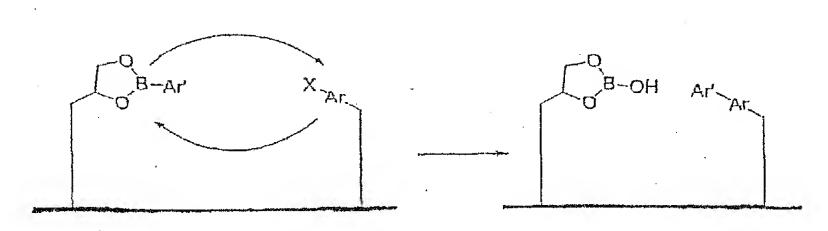
Z* = Aryl, hetaryl, NR or O or S etc

 $M = e.g. BR, BR_2$, SnR_2 etc.

R = H, alkyl, aryl, hetaryl, OR, NR₂

 $M^* = e.g. B(OH)R, B(OH)R_2^*, Sn(OH)R_2 etc.$

FIG. 6R. Arylation Biaryl formation by the reaction of Borates with Aryls or Heteroaryls



X = Halogen, OMs, OTf, OTos, etc

FIG. 6S. Arylation Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls

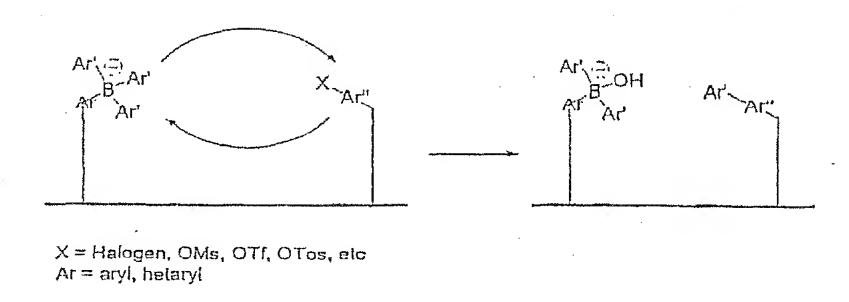


FIG. 6T. Arylation Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls

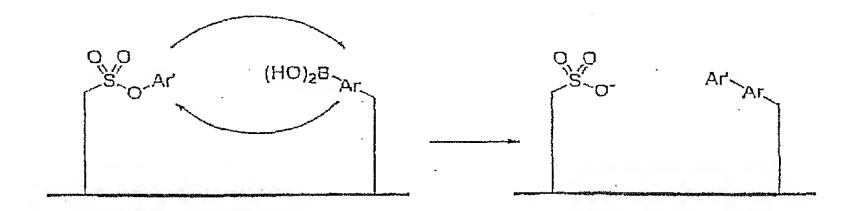
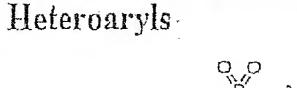


FIG. 6U. Arylation

Arylamine formation by the reaction of amines with activated Aryls or



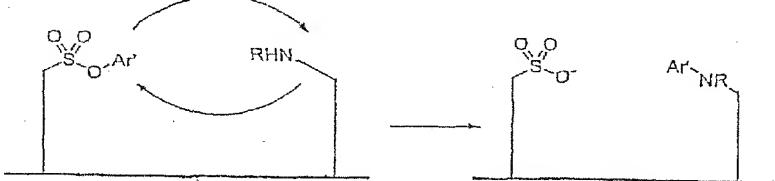


FIG. 6V. Arylation

Arylamine formation by the reaction of amines with hypervalent iodonium salts

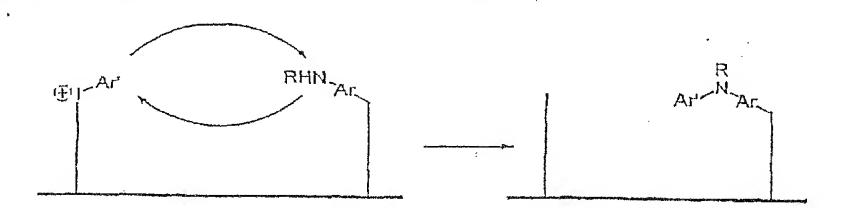
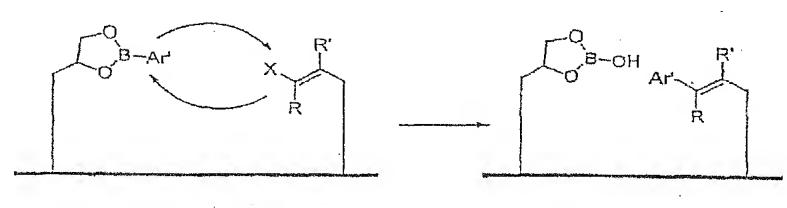


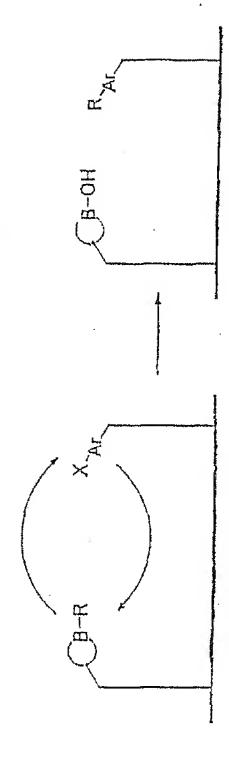
FIG. 6X. Arylation

Vinylarene formation by the reaction of alkenes with Aryls or Heteroaryls



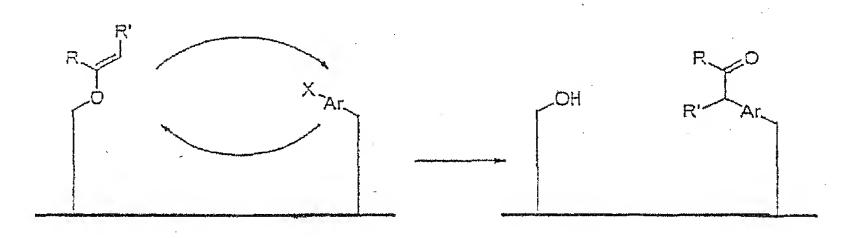
X = Halogen, OMs, OTf, OTos, etc

FIG. 6Y. Alkylation
Alkylation of arenes/hetarens by the reaction with Alkyl boronates



X = Halogen, OMs, OTf, OTus, etc

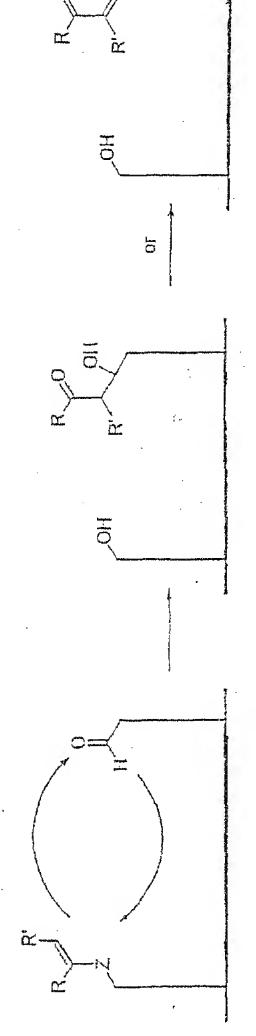
FIG. 6Z. Alkylation Alkylation of arenes/hetarenes by reaction with enolethers



X = Halogen, OMs, OTf, OTos, etc

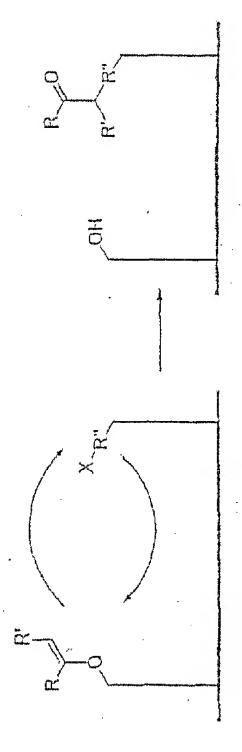
Nucleophilic substitution using activation of nucleophiles

FIG. 6AA. Condensations Alkylation of aldehydes with enolethers or enamines



Z = NR, O; X = Halogen, OMs, OTI, OTos, etc

FIG. 6AB. Alkylation Alkylation of aliphatic halides or tosylates with enolethers or enamines



X = Halogen, OMs, OTf, OTos, etc

Cycloadditions

FIG. 6AC. [2+4] Cycloadditions

$$R_3 \xrightarrow{R_2 R_1 R_g}$$

$$R_3 \xrightarrow{R_2 R_1 R_g}$$

$$R_6 \xrightarrow{R_4 R_5}$$

$$Z = 0, NR$$

FIG. 6AD. [2+4] Cycloadditions

Y = CN, COOR, COR, NO_2 , SO_2R , S(=0)R, SO_2NR_2 , F

FIG. 6AE. [3+2] Cycloadditions

$$R_1$$
 R_2 $O_{0} = S_1$ N_1 N_2 N_3 N_4 N_5 $N_$

Y = CN, COOR, COR, NO2, SO2R, S(=0)R, SO2NR2, F

FIG. 6AF. [3+2] Cycloadditions

Y = CN, COOR, COR, NO₂, SO₂R, S(=0)R, SO₂NR₂, F

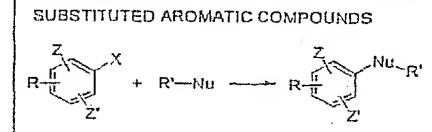
FIG. 7A. Pairs of reactive groups X, Y and the resulting bond XY.

Nucleophille substitution reactions

		ITHUAMINES	AMDES		THIOAMIDES	OXIMES	SULFONAMIDES	DI-AND TRI- FUNCTIONAL COMPOUNDS	D& AND TRI- FUNCTIONAL COMPOUNDS	7"z, COO", R"z, CN', sch.
The second secon	R A R"-NH, P	0-R' HIV-R"	R-C + R"-NH2 R-C	H	RA + R"-MH2 R-	R. A. T. R.	R'-502CI + R'N'-R' H'502-N	$R'-X$ + $R-\frac{Z'}{\zeta}$ $R-\frac{Z'}{\zeta}$	$R' - \begin{cases} + R - \frac{Z'}{2} \\ + R - \frac{Z'}{2} \end{cases}$	$Z'.Z = COOR$, CHO, COR, CONR'z, NO_2 , SOR, SO ₂ H, SO ₂ HR'z,
	ETHERS	THIOETHERS	sec-AMINES	terl-AMINES	()-HYDROXY ETHERS	p-HYDROXY THIOETHERS	B-HYDROXY AMINES	p-AMINO ETHERS	AMIDES	AMIDES
	R-0-R'	R-S-R'	R-N-R'	R -N-R' R-R	HQ 0H;	HO SH	里十	RHN OR	R-K	HIV-R"
	R-X + R'-0'	R-X + R'5	R-X + R'-11H2	R-X + R-H-R'	0 + R-0.	0 + R'-S'	10 + R'-WH2	N + R-0	0 + R"—///H2 -	5-R" + R"-MH2
			······································		1	<u>}</u>			Ċ	Ė

FIG. 7B

Aromatic nucleophilic substitution



. Nu = Oxygen-, Nilrogen-, Sulfur- and Carbon Nucleophiles X = F, Cl. Br. I, OSO_2CH_3 , OSO_2CF_3 , OSO_2TOL , , etc. Z'.Z = COOR, CHO, COR, CONR"₂, CDO", CN, NO_2 , SOR, SO_2R , $SO_2NR"_2$, ect.

FIG. 7C Transition metal catalysed reactions

FIG. 7D Addition to carbon-carbon multiple bonds

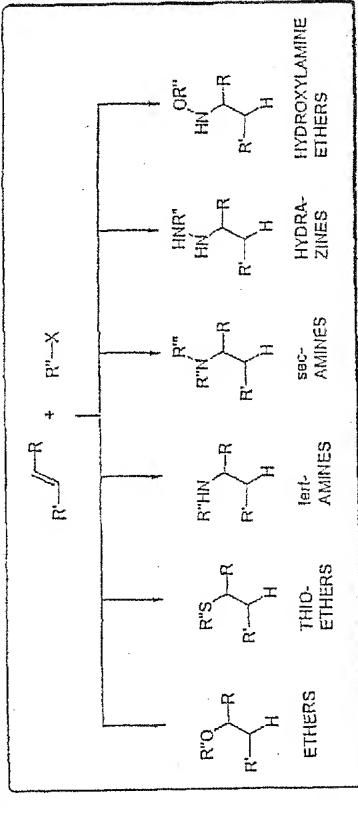


FIG. 7E

z = z FUNCTIONAL z FUNCTIONAL z ALKENES	Z = H, Alkyl, Ar, Z' = Z', Alkyl, Ar, Z' = COOR, C10, COR, CONR'2, CN, NO2, SOR, SO2R, SO2NR'2, ect.
$\left\{\begin{array}{cccccccccccccccccccccccccccccccccccc$	$Z = H$, Alkyl, Z', Ar $Z'' = COOR$, CHO, COR, CONR" ₂ , CN, NO_2 , SOR, SO ₂ R, SO ₂ NR" ₂ ect. $Z' = Z''$ $R = R'_1 = R''_2 = Z$

FIG. 7F Cycloaddition to multiple bonds

SUBSTITUTED	SUBSTITUTED CYCLOALKENES	CN, NO ₂ , 1, SO ₂ R elc. CR ₂ , S,
R R O R R C R R O R R R R O R R R R R O R R R R R O R R R R R O R R R R R O R R R R R O R R R R R O R R R R R O R R R R R O R R R R R O R R R R R O R R R R R R O R R R R R R O R R R R R R O R R R R R R O R R R R R R O R R R R R R R R R R R R O R	A X X X X X X X X X X X X X X X X X X X	Z.=COOR, CHO, COR, COOH COAr CN, NO ₂ , Ar, CH ₂ OH, CH ₂ NH ₂ , CH ₂ CN, SOR, SO ₂ R elc. R = H, Alkyl, Ar, Z $X=0$, NR, CR ₂ , S,
SUBSTITUTED CYCLOALKENES	SUBSTITUTED CYCLODIENES	SUBSTITUTED 1,2,3-TRIAZOLES
$\begin{bmatrix} Z & R & R \\ R^{i} & R & R^{i} \end{bmatrix}$	R. R	2—————————————————————————————————————
x x x + x	ж—— ж +	Z-Z-Z-Z-Z-Z-Z-Z-Z-Z-Z-Z-Z-Z-Z-Z-Z-Z-Z-

FIG. 7G Addition to carbon-hetero multiple bonds

Substituted	Subslituted Alkenes	, SOR, Aryl	0 ₂ , ect.	
H' R"	To Ho	COOR, CHO, COR, CONR"2, CN, NO2,SOR SO2R, SO2NR"2, ect. R" = H, Alkyl, Aryl	R, SOR, SO ₂ R, CN, N	
R"0-6-4 R" + R" R	+ H	Z,'Z' = COOR, CHO, COR, CONR"2, CN, NO2,SOR, SO2R, SO2N"2, ect. R" = H, Alkyl, Aryl	Z = COOR, CHO, COR, SOR, SO ₂ R, CN, NO ₂ , ect. R = R', H, Alkyl, Ar,	R" = R", H, Alkyl, COR,
β-Hydroxy Ketones β-Hydroxy Aldehydes	Vinyl Kelanes Vinyl Aldehydes	Subsituted Alkanes	R' Subsiffuled Z Amines	Substituted NH Amines R
R. R. R.	X X X	R. Z.	H. R.	NaBH ₃ CN R'
R' R + R" R	R' CO + R'' CO	Z' Z + R' KR	Z R'' + CH ₂ O + R'''	R-NH ₂ + 0

Figure 8. Cleavable Linkers

FIG. 8A. Linker for the formation of Ketones, Aldehydes, Amides and Acids

$$R^{m}$$
 R^{m}
 R^{m

FIG. 8B. Linker for the formation of Ketones, Amides and Acids

$$R$$
 NO_2
 NO_2
 NO_3
 NO_4
 NO_4

FIG. 8C. Linker for the formation of Aldehydes and Ketones

FIG. 8D. Linker for the formation of Alcohols and Acids

FIG. 8E. Linker for the formation of Amines and Alcohols

FIG. 8F. Linker for the formation of Esters, Thioesters, Amides and Alcohols

FIG. 8G. Linker for the formation of Sulfonamides and Alcohols

FIG. 8H. Linker for the formation of Ketones, Amines and Alcohols

$$R' \downarrow 0$$
 $R' \downarrow 0$
 $R' \downarrow 0$
 NO_1
 $R' \downarrow 0$
 NO_2
 $R' \downarrow 0$
 NO_3
 NO_4
 NO_4

FIG. 8I. Linker for the formation of Ketones, Amines, Alcohols and Mercaptanes

R' NO₂ hv R' NO + HX-R
$$\times$$
 = 0, S, NH, NF

FIG. 8J. Linker for the formation of Biaryl and Bilietaryl

FIG. 8K. Linker for the formation of Benzyles, Amines, Anilins Alcohols and Phenoies

FIG. 8L. Linker for the formation of Mercaptanes

TCER = Iris(2-carboxyelly/)phosphine

FIG. 8M. Linker for the formation of Glycosides

FIG. 8N. Linker for the formation of Aldehydes and Glyoxylamides

FIG. 80. Linker for the formation of Aldehydes, Ketones and Aminoalcohols

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